IN THE CLAIMS:

Please amend the claims and add new claims 627-648 as shown below.

1-598. (Previously cancelled)

599. (Original) A method of detecting nucleic acid in a sample, the nucleic acid having at least two portions, said method comprising:

providing a substrate having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a first portion of the sequence of a nucleic acid to be detected;

providing a scattered light detectable nanoparticle probe having oligonucleotides attached thereto, the oligonucleotides bound to the nanoparticle probe having a sequence complementary to a second portion of the sequence of said nucleic acid wherein the oligonucleotides are attached to the nanoparticles in a stepwise ageing process comprising (i) contacting the oligonucleotides with the nanoparticles in a first aqueous solution for a period of time sufficient to allow some of the oligonucleotides to bind to the nanoparticles; (ii) adding at least one salt to the aqueous solution to create a second aqueous solution; and (iii) contacting the oligonucleotides and nanoparticles in the second aqueous solution for an additional period of time to enable additional oligonucleotides to bind to the nanoparticles;

contacting said nucleic acid, the substrate and the aggregate probe under conditions effective to allow hybridization of said nucleic acid with the oligonucleotides on the nanoparticle probe and with the oligonucleotides on the substrate and form a light scattering complex bound to the substrate

illuminating the light scattering complex under conditions effective to produce scattered light from said complex;

detecting the light scattered by said complex under said conditions as a measure of the presence of the nucleic acid.

600. (Original) The method of Claim 599 wherein said nucleic acid is contacted with the substrate so that said nucleic acid hybridizes with the oligonucleotides on the substrate, and said nucleic acid bound to the substrate is then contacted with the scattered light detectable nanoparticle probe so that said nucleic acid hybridizes with the oligonucleotides on the nanoparticle probe.

601. (Original) The method of Claim 599 wherein said nucleic acid is contacted with the nanoparticle probe so that said nucleic acid hybridizes with the oligonucleotides on the nanoparticle probe, and said nucleic acid bound to the nanoparticle probe is then contacted with the substrate so that said nucleic acid hybridizes with the oligonucleotides on the substrate.

602. (Original) The method of Claim 599 wherein said nucleic acid is contacted simultaneously with the nanoparticle probe and the substrate.

603. (Original) The method of Claim 599 wherein the substrate has a plurality of types of oligonucleotides attached to it in an array to allow for the detection of multiple portions of a single nucleic acid, the detection of multiple different nucleic acids, or both.

604. (Currently amended) The method [according to] of Claim 599 wherein said substrate is a waveguide comprising (a) a transparent element having a refractive index greater than that of the fluid sample; (b) a light receiving edge; and (c) a surface having oligonucleotides bound thereto.

605. (Currently amended) The method [according to] of claim 604 wherein the illuminating is performed at the light receiving edge of the waveguide with light effective to create total internal reflection within the waveguide, thereby [simulataneously illuminating] providing excitation energy to the entire surface of the waveguide via an evanescent wave.

606. (Original) The method according to claim 603, wherein a plurality of different types of nanoparticles with different sizes or compositions or both are distinguishably detected, each type of nanoparticles specifically associating with a different nucleic acid sequence.

607. (Currently amended) A method of detecting two or more nucleic acids in a sample, each nucleic acid having at least two portions, the method comprising:

providing a substrate having two or more types of oligonucleotides attached thereto, [each type of oligonucleotides attached to a different place on the substrate and] each type of oligonucleotides having sequences complementary to a first portion of the sequences of one of nucleic acids to be detected;

providing two or more types of scattered light detectable nanoparticle probes, each type of nanoparticle probes having [the] oligonucleotides bound thereto, the oligonucleotides bound to each type

of probe have a sequence that [are] is complementary to a second portion of the sequence of one of said nucleic acids to be detected, wherein the oligonucleotides are attached to the nanoparticles in a stepwise ageing process comprising (i) contacting the oligonucleotides with the nanoparticles in a first aqueous solution for a period of time sufficient to allow some of the oligonucleotides to bind to the nanoparticles; (ii) adding at least one salt to the aqueous solution to create a second aqueous solution; and (iii) contacting the oligonucleotides and nanoparticles in the second aqueous solution for an additional period of time to enable additional oligonucleotides to bind to the nanoparticles;

contacting said nucleic acids, the substrate and the nanoparticle probes under conditions effective to allow hybridization of said nucleic acids with the oligonucleotides on the nanoparticle probes and with the oligonucleotides on the substrate to form a light scattering complex bound to the substrate;

illuminating the light scattering complex under conditions effective to produce scattered light from said complex; and

detecting the light scattered by said complex under said conditions as a measure of the presence of one or more nucleic acids.

608. (Original) The method of Claim 607 wherein said nucleic acids are contacted with the substrate so that said nucleic acids hybridize with the oligonucleotides on the substrate, and said nucleic acids bound to the substrate are then contacted with the scattered light detectable nanoparticle probes so that said nucleic acids selectively hybridize with the oligonucleotides on the nanoparticle probes.

609. (Original) The method of Claim 607 wherein said nucleic acids are contacted with the nanoparticle probes so that said nucleic acids hybridize with the oligonucleotides on the nanoparticle probes, and said nucleic acids bound to the nanoparticle probes are then contacted with the substrate so that said nucleic acids hybridize with the oligonucleotides on the substrate.

610. (Original) The method of Claim 607 wherein said nucleic acids are contacted simultaneously with the nanoparticle probes and the substrate.

611. (Original) The method of Claim 607 wherein the substrate has a plurality of types of oligonucleotides attached to it in an array to allow for the detection of multiple portions of a single nucleic acid, the detection of multiple different nucleic acids, or both.

612. (Original) The method according to Claim 607 wherein said substrate is a waveguide comprising (a) a transparent element having a refractive index greater than that of the fluid sample; (b) a light receiving edge; and (c) a surface having oligonucleotides bound thereto.

613. (Currently amended) The method according to [claim] Claim 612 wherein the illuminating is performed at the light receiving edge of the waveguide with light effective to create total internal reflection within the waveguide, thereby [simultaneously illuminating] simultaneously providing excitation energy to the entire surface of the waveguide via an evanescent wave.

614. (Currently amended) The method of any one of Claims 599 or 607 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

615. (Currently amended) The method of any one of Claims [claim] 599 or 607 wherein the nanoparticles are gold nanoparticles.

616. (Currently amended) The method of any one of Claims 599 or 607 wherein the oligonucleotides to be bound to the nanoparticles have covalently bound thereto a moiety comprising a functional group that can bind to the nanoparticles.

617. (Currently amended) The method of [Claims 599 or 607] Claim 616 wherein the moiety comprises a thiol, a polythiol, or a cyclic disulfide group.

618. (Currently amended) The method of any one of Claims 599 or 607 wherein all of the salt is added to the first aqueous solution in a single addition.

619. (Currently amended) The method of any one of Claims 599 or 607 wherein the salt is added gradually over time.

620. (Currently amended) The method of any one of Claims 599 or 607 wherein the salt is solected from the group consisting of sodium chloride, magnesium chloride, potassium chloride, ammonium chloride, sodium acetate, ammonium acetate, lithium chloride, tetramethylammonium chloride, a combination of two or more of these salts, one of these salts in a phosphate buffer, and a combination of two or more of these salts in a phosphate buffer.

621. (Currently amended) The method of [claim] Claim 619 wherein the salt is sodium chloride in a phosphate buffer.

622. (Currently amended) The method of any one of Claims 599 or 607 wherein the nanoparticles have a diameter ranging between about 10 and about 100 nm.

623. (Currently amended) The method of any one of Claims 599 or 607 wherein the nanoparticles have a diameter of about 50 nm.

624. (Currently amended) The method of any one of Claims 599 or 607 wherein the nanoparticles have a diameter of about 100 nm.

625. (Currently amended) The method of any one of Claims 599 or 607 wherein two scattered light detectable nanoparticle probes of different diameters are used.

626. (Currently amended) The method of [claim 624] Claim 625 wherein the nanoparticle probes have a diameter of 50 nm and 100 nm.

627. (New) The method of any one of Claims 599 or 607 wherein the second aqueous solution has an ionic strength sufficient to overcome at least partially the electrostatic attraction or repulsion of the oligonucleotides for the nanoparticles and the electrostatic repulsion of the oligonucleotides for each other.

628. (New) The method of any one of Claims 599 or 607 wherein the oligonucleotides are bound to the nanoparticles through sulfur linkages.

629. (New) The method of any one of Claims 599 or 607 wherein the oligonucleotides and nanoparticles are contacted in aqueous solution for about 12 to about 24 hours.

630. (New) The method of any one of Claims 599 or 607 wherein salt is added to the aqueous solution to form the aqueous salt solution that is buffered at pH 7.0 and that contains about 0.1 M NaCl.

631. (New) The method of any one of Claims 599 or 607 wherein the oligonucleotides and nanoparticles are contacted in the salt solution for an additional 40 hours to increase the density of oligonucleotides bound to the nanoparticles.

632. (New) The method of any one of Claims 599 or 607 wherein the oligonucleotides are present on a surface of the nanoparticles at a surface density of at least 10 picomoles/cm^2.

633. (New) The method of Claim 632 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 15 picomoles/cm^2.

634. (New) The method of Claim 633 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of from about 15 picomoles/cm^2 to about 40 picomoles/cm^2.

635. (New) The method of any one of Claims 599 or 607 wherein the oligonucleotides bound to the nanoparticles comprise at least one type of recognition oligonucleotides, each type of the recognition oligonucleotides comprising a spacer portion and a recognition portion, the spacer portion being designed so that it can bind to the nanoparticles.

636. (New) The method of Claim 635 wherein each of the spacer portions of the recognition oligonucleotides has a moiety covalently bound thereto, the moiety comprising a functional group which can bind to the nanoparticles.

637. (New) The method of Claim 635 wherein the spacer portion comprises at least about 10 nucleotides.

638. (New) The method of Claim 637 wherein the spacer portion comprises from about 10 to about 30 nucleotides.

639. (New) The method of Claim 638 wherein the bases of the nucleotides of the spacer are all adenines, all thymines, all cytosines, all uracils, or all guanines.

640. (New) A method of any one of Claims 599 or 607 wherein the oligonucleotides bound to nanoparticles comprise at least one type of recognition oligonucleotides and at least one type of diluent oligonucleotides.

641. (New) The method of Claim 640 wherein each of the recognition oligonucleotides comprises a spacer portion and a recognition portion, the spacer portion being designed so that it can bind to the nanoparticles.

642. (New) The method of Claim 641 wherein each of the spacer portions of the recognition oligonucleotides has a moiety covalently bound thereto, the moiety comprising a functional group which can bind to the nanoparticles.

643. (New) The method of Claim 641 wherein the spacer portions of the recognition oligonucleotides comprises at least about 10 nucleotides.

644. (New) The method of Claim 643 wherein the spacer portions of the recognition oligonucleotides comprises from about 10 nucleotides to about 30 nucleotides.

645. (New) The method of Claim 641 wherein the bases of the nucleotides of the spacer are all adenines, all thymines, all cytosines, all uracils or all guanines.

646. (New) The method of Claim 640 wherein the diluent oligonucleotides contain about the same number of nucleotides as are contained in the spacer portions of the recognition oligonucleotides.

647. (New) The method of Claim 646 wherein the sequence of the diluent oligonucleotides is the same as the sequence of the spacer portions of the recognition oligonucleotides.

648. (New) The method of Claim 640 wherein the oligonucleotides comprise at least two types of recognition oligonucleotides.